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SOME BIOLOGICAL APPLICATIONS OF ORGANOMETALLIC COMPOUNDS[1]

By Professor HENRY GILMAN

IOWA STATE COLLEGE

ORGANOMETALLIC compounds are compounds which have a metal directly attached to carbon, and are conveniently designated by the formula RM where M is a metal. They fall into three broad groups: those which are highly reactive *chemically,* like organopotassium compounds; those of moderate reactivity, such as organolithium and organomagnesium compounds; and those of relatively low reactivity, like the organomercury and organobismuth types.

Only those organometallic compounds of low chemical reactivity find any immediate biological application. It is out of the question, for example, to use organopotassium compounds directly, for they are not only spontaneously inflammable but react violently with water and carbon dioxide; and both violently and indiscriminately with the organic materials that go to make up cells.

However, it is probable that reactive types like those of magnesium (the Grignard reagents) and those of lithium are of greatest biological significance not because of their effects on body cells and fluids but because of the uncommon service they give to an understanding of biologically active material. There is hardly a branch of biologically active organic compounds (like vitamins, hormones, carcinogens) wherein RM compounds have not been used in one way or another to throw light on reaction mechanisms and procedures concerned with the structure and preparation of such compounds. It is doubtful if any class of organic compounds exceeds the reactive

[1] Address of the retiring vice-president and chairman of the Section on Chemistry, American Association for the Advancement of Science, December 27, 1940.

RM types in versatility of reaction, particularly from the viewpoint of synthesis. Interestingly enough, some of the methods of choice for synthesis of the immediately important, less reactive RM compounds involve the use of the more reactive RM types. As an illustration, many organomercury compounds are best prepared from organomagnesium or organolithium compounds.

Organometallic compounds have not been prepared from all the metals. It is highly probable, however, that all types of RM compounds will be prepared. The history of organometallic compounds shows that hypotheses postulating the non-formation of some RM types have undergone repeated revision necessitated by the preparation of organometallic compounds, the possible existence of which has been denied. At one time or another practically all the lesser reactive RM types have been examined for a great variety of biological action. Out of these studies have come some highly important applications, and promises of other significant biological uses.

The beneficial use of metals and their inorganic compounds in medicine dates back hundreds of years. Organometallic compounds, on the other hand, are relatively new. The biological action of metals and inorganic salts may differ markedly from organometallic compounds which are, in many respects, also salt-like in character. A bridge connecting inorganic materials with organometallic compounds is the class of compounds known as the metallic hydrides. Actually, these hydrides may be considered formally as the first members of the organometallic homologous series. For example, if one adds to sodium hydride (NaH) the constant of homology (CH_2) there results methylsodium (CH_3Na) or the simplest true organosodium compound in that homologous series.

The hydrides, such as arsine (AsH_3) and tin hydride (SnH_4), are characterized by general extreme toxicities. With the introduction of CH_2 groups the toxicity tends to decrease, but the simpler organometallic compounds are definitely and characteristically poisonous. The decrease in toxicity as one goes from the metallic hydrides to the simpler organometallic compounds points the way to the synthesis of organometallic compounds sufficiently toxic for invading organisms and adequately tolerated by the host. The various reactions at the disposal of the organic chemist now make it possible to convert a highly toxic, relatively simple organomercury compound, for example, to an organomercury compound which is relatively safe and effective. The necessary transformations are somewhat simple in character, and involve alterations in the architecture of a molecule by appropriate variations of the kind, number and arrangement of groups. The actual operations may initially be quite difficult because of the special chemistry involved with many organometallic compounds. However, when proper conditions have been devised, the possibilities of preparing large numbers of compounds are essentially unlimited. This is a fortunate circumstance, because the paucity of information correlating physiological action with chemical constitution demands a large amount of empirical work, and the synthesis of a great number of compounds. An historically important illustration is Ehrlich's "606" for the treatment of syphilis.

As a consequence of this necessary "trial and error" approach there have evolved the beginnings of some relatively amorphous generalizations on chemical constitution and physiological action. Biologists are peculiarly appreciative and sympathetic of the gropings of the chemist, because of the astonishing differences between animate and inanimate matter. Both, however, are moving in the idealistic direction of achieving formulations which will be so exact that accurate predictions can be made. The goal, however, is so very distantly removed that they don't waste time considering that with the ultimate fruition of their efforts they will have succeeded in transforming science to bookkeeping, by the simple process of making science extinct when there is no further need to devise and interpret experiments.

Time does not permit a detailed accounting of the immediate biological applications of organometallic compounds. In human medicine, organometallic compounds of mercury have been used as antiseptics, for the treatment of syphilis, and as diuretics. The arsenic, antimony and bismuth compounds have found wide applications in a variety of protozoan diseases. Organogold compounds have been used, with indifferent success, in the treatment of tuberculosis; but with greater promise in the treatment of some forms of arthritis. Recent studies indicate that organolead compounds following the earlier and somewhat abortive work on the use of colloidal lead, may be beneficial in the treatment of cancer. Currently, germanium compounds are being examined in studies on pernicious anemia.

In veterinary medicine it is now being established that, among other applications, organic compounds of arsenic and bismuth are effective in the treatment of some forms of coccidiosis. In botany, organomercury compounds are used extensively as seed disinfectants to prevent smut diseases of cereals. Little work has been done with organometallic compounds in entomology, partly because of a trend to avoid the use of metals and partly because of cost. Neither of these objections may be serious with future developments. Practically nothing has been done directly in genetics. However, some studies indicate that muta-

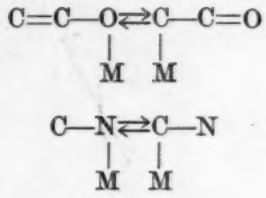
tions have been effected, in very low rates, with Drosophila by means of salts of metals. The highly selective and preferential reactions of organometallic compounds may make possible mutations by chemical agents.

The pronounced effects of very small quantities of metals and their derivatives have given rise to the expression "oligodynamic action." For example, 1 part of copper in 100,000,000 parts of distilled water will kill algae. Metals or their salts are widely distributed in plants and animals, and the importance of traces of metals in nutrition is common knowledge. Some metals like copper and zinc are normal constituents of the human brain, and are perhaps necessary for normal functioning. Traces of copper and cobalt assist iron in maintaining a steady formation of haemoglobin in the cure of anemia; and copper appears to be particularly necessary for the formation and maintenance of cytochrome oxidase activity of some tissues.

The pronounced effect of small amounts of metals is initmately associated with enzymes. A case can be made for the concept that any substance which is present in traces in the cell *and* which is apparently necessary in the diet or medium must either be an essential part of some enzyme or the enzyme itself. The trace metals which may be necessary for normal functioning of cells are copper, cobalt, zinc and manganese; and these metallic combinations appear to function as prosthetic groups in enzymes. It may be attractive, speculatively, to pursue the idea of enzyme-like action of certain synthetic drugs, minute amounts of which are profoundly effective. We refer here to synthetics which are not normal constituents of cells but which may become transitorily prosthetic groups of enzymes. One may expect confidently that the expanding use of the tracer element technique, particularly with radioactive metal combinations, will throw new light on the biological transformations of metallic substances.

It may properly be asked: "What relationship exists between metals and their inorganic salts and organometallic compounds?" We know that it is possible to convert some inorganic materials biologically to organometallic types. Tellurium is methylated in the body and exhaled as the offensive dimethyltellurium. Molds will also methylate inorganic compounds of arsenic and tellurium to the corresponding organometallic compounds. Relatively little is known of the mechanism of biological action of metallic types. There may or may not be an intermediary and transitory formation of organometallic or pseudo-organometallic compounds, although it is possible, in the laboratory, to prepare organometallic compounds by interaction of organic compounds with metals or their inorganic salts. Even if true organometallic compounds are not involved in biological transformations, there are good reasons for believing that in a number of cases organic compounds are formed in which the metal is bound not necessarily to carbon (to give a true organometallic compound) but to oxygen, sulfur or nitrogen. The type of metal linkage in such cases may be coordinate.

Recent studies have shown that numerous organic compounds having a metal attached to oxygen or nitrogen behave in many respects as though the metal were attached to carbon. The rearrangements involved may be illustrated simply by the following:



The extent of these and other equilibria varies with the particular system of elements involved. However, the observations that some organic compounds having a metal attached presumably to an element other than carbon may function as a true organometallic compound in which the metal is attached to carbon are of paramount importance. The applicability of this concept is significant not only from a strictly chemical aspect but also from the viewpoint of two of the most important biological materials; chlorophyll and haemoglobin.

Willstätter has suggested that the magnesium linkage in chlorophyll may resemble that present in Grignard reagents and be a significant point of reaction with carbon dioxide in photosynthesis. One may then speculate that some of the subsequently necessary reductions and condensations leading to carbohydrates may also involve known Grignard-like transformations. It is interesting to recall that quite recent studies show the formation of carboxylic acids in photosynthesis, for a primary reaction between Grignard reagents and carbon dioxide is the formation of carboxylic acids. To continue speculatively, the other biologically important catalyst, haemoglobin, may function as an oxygen carrier, possibly by means of peroxide formation due to an organoiron complex or its equivalent.

There are, then, three important classes of biological applications of organometallic compounds: (1) The almost indispensable use of organometallic compounds in the determination of structure and the synthesis of biologically significant materials like vitamins and hormones. (2) The direct application of organometallic compounds in the treatment of infections and diseases of both plants and animals. (3) The

apparent organometallic characteristics of two basically important materials in plant and animal transformations: chlorophyll and haemoglobin. It seems altogether reasonable to predict that expanding knowledge in the relatively young field of organometallic chemistry will assist materially in advancing our understanding of biological processes and in further controlling various plant and animal diseases.

THE MOTIONS OF THE STARS[1]

By Dr. EVERETT I. YOWELL

PROFESSOR EMERITUS OF ASTRONOMY, UNIVERSITY OF CINCINNATI

THE first observational evidence of stellar motions was given by Sir Edmund Halley[2] in 1718. Comparing the positions of the Almagest with recent observations to determine the precession, he found large changes in the latitudes of Sirius, Arcturus, Aldebaran and Betelguese; he considered these too great to be attributed to errors of observation or reduction and decided that these stars had a motion of their own.

The proper motion is an angle and we need the distance of the star to convert it into linear motion at right angles to the line of sight. The radial velocity is also needed to give the motion with reference to the sun.

If we accept the estimate that errors of observation did not exceed 15′ at the time of Copernicus; that Tycho reduced this limit to 2′ or 3′ and that Flamsted reduced it to 5″, we see how difficult it was to detect any small proper motions in less than a century.

By the end of the eighteenth century we have some proper motions in Maskelyne's "Catalogue of 36 Fundamental Stars" and in Mayer's "Catalogue of 80 Stars." Mayer obtained his motions by comparing his observations with those made by Roemer fifty years earlier.

Sir William Herschel[3] in 1783 used seven of these motions to determine the motion of the sun. He based his method on the fact that the solar motion would impart a parallactic component to each star, in a great circle passing through the star and the apex of the sun's motion. Drawing these great circles, he found that their intersections clustered in and around the constellation Hercules, with the mean point near λ Herculis; this he adopted as the solar apex. He checked this position with Mayer's motions and found 32 favorable and 12 unfavorable to his hypothesis.

Herschel[4] again considered the problem in 1805; he found a provisional apex from six stars of Maskelyne's Catalogue; then modified it by comparison with the other stars of that catalogue. This new value differed from the other by 16° in right ascension and 23° in declination.

Bessel increased the number of known proper motions by reducing the observations of Bradley and comparing them with the results of Piazzi and himself. With the better determined of these motions, he tested the hypothesis of Herschel by a different method. He[5] plotted the poles of the great circles in which these motions took place and found they were scattered all over the sky. Were they largely parallactic, they should have been concentrated along the great circle whose pole was the solar apex. His results did not agree with Herschel's.

Argelander was the first to observe a list of stars, limited to those suspected of having proper motions. His Abo Catalogue of 560 stars contained 390 whose centennial motions exceeded 10″. From these he determined the apex[6]; 259° = A, 32° = D. His method was to compute the position angle of each motion and compare it with the position angle of the parallactic motion with respect to an assumed apex. His equations were based on the assumption that directions of motion were at random. His result confirmed Herschel's and convinced astronomers that the solar motion was real.

Airy[7] published his method in 1859; he resolved the stellar motions along three rectangular axes. When the components were summed he assumed the peculiar motions would cancel, leaving the parallactic components to sum up into those of the solar motion. In Airy's method it was also necessary to make some assumption concerning the distance of the stars. In general the amount of proper motion was assumed to be a better criterion of distance than the visual magnitude.

Thus Stumpe[8] divided his 1,054 proper motions into four groups according to the size of the proper motions; in the first group of 551 stars, he took $.''16 < \mu < .''32$; in the next group of 340 stars, the limits were .″32 and .″64; in group 3 (105 stars) the limits were .″64 and 1.″28; and the last group had 58

[1] Address of the retiring vice-president and chairman of the section of astronomy of the American Association for the Advancement of Science, Philadelphia, December 31, 1940.

[2] *Phil. Trans.*, 6, 329–330.

[3] Scientific Papers of Sir William Herschel, 1, 108–130.

[4] *Idem*, 2, 317–337.

[5] "Fundamenta Astronomiae," 308–313.

[6] A.N., 16, 45.

[7] *Mem. Royal Astron. Soc.*, 28, 143.

[8] A.N., 125, 385–430.

stars whose motion exceeded 1.″28 per annum. The values of A were sufficiently concordant, but those of D were discordant, ranging from 42° for the smallest motions down to 30° for the greatest motions.

Dr. Porter[9] repeated the solution, using similar limits and similar groups, but his 1,340 motions were taken from his own Cincinnati Catalogue. His results were similar; good agreement in A, but disagreement in D; his values of D had a greater range—from 54° to 35°. Porter's comment that "the evidence for a common drift of the nearer stars seems to be strong" calls attention to the probability that the underlying hypothesis that motions are at random may be invalid.

We must notice some of the difficulties faced by those who computed proper motions. The earlier observations were subject to large accidental errors as well as systematic ones; among these were errors in refraction, precession, aberration, nutation and fundamental star positions, not to mention instrumental peculiarities. Bessel devised ways of determining the instrumental imperfections and correcting them. The constants were improved by successive approximations as more material became available. The list of fundamental stars was improved by increasing the number of stars in it and also increasing the precision of their positions; but our most important systems—Boss, Eichelberger and FK3—are not yet in complete harmony.

The great number of star catalogues that appeared in the nineteenth century furnished many positions at different epochs, but only the bright stars were well observed. To supply this deficiency, the Astronomische Gesellschaft planned to observe all stars brighter than the 9th magnitude and determine their positions for 1875.0. Not all of the participants finished their work on time, and some of the catalogues were issued early this century for the epoch 1900.0. A greater work was planned for 1900.0– to determine the positions by photography of all stars down to the 11th magnitude; some zones of this Astrographic Catalogue are still incomplete.

Small proper motions of poorly observed stars are unreliable, due to the errors of the positions on which they depend. Computers of the solar motion frequently reject these, although they run the risk of a systematic error in their apex.

We must note that certain assumptions had to be made in handling this problem of the solar motion. Quite generally it was assumed that the *motus peculiares* of the stars were haphazard in direction and so would neutralize one another when large groups were considered. Some assumption as to distance also had to be made, especially in Airy's method. How much these assumptions might invalidate the result could not be determined.

[9] A.J., 12, 93.

Let us turn back to our second unknown quantity, the distances of the stars. Bessel[10] published the parallax of 61 Cygni in 1838. The number of parallaxes grew slowly until the introduction of the photographic method. At the end of the century less than 100 reliable parallaxes were known. Schlesinger's work at Yerkes is especially noteworthy in developing the method of obtaining reliable photographic parallaxes, and our American observatories have contributed largely to our knowledge of parallaxes. These are trigonometric parallaxes; to them must be added those determined in other ways, such as spectroscopic and dynamical parallaxes. With these we change our proper motions into linear motions; they also enable us to correct our assumptions as to the distances of the stars in our solar motion problem.

The second component of a star's motion—the motion in the line of sight—remained unknown until the discovery and application of the laws of spectroscopy, especially the Doppler-Fizeau principle. Shortly after Kirchhoff announced his results, some astronomers began to apply them to stellar objects. Progress was slow until photographic methods had replaced visual ones. Our first reliable and extensive catalogue of radial velocities was that of Campbell at Lick.[11] During this century there has been a continual increase in the number of radial velocities available, and again we are indebted to American observatories for a great number of these results.

The variable proper motions of Sirius and Procyon led Bessel to predict their duplicity. The orbits, computed for the unseen companions, proved satisfactory after these were discovered.

Some members of the Pleiades have a common proper motion; so do five stars in the Big Dipper. An early investigation of the Taurus cluster (Hyades group) was made by Lewis Boss[12]; he found 39 stars that shared this common motion toward the vertex $A = 92°$, $D = 7°$, moving through space with a common velocity of 46 km per second. R. E. Wilson in 1932 found 136 stars to be members of this moving cluster, and 221 more were members of the group.

Klinkerfues in 1878 found the convergent of the five stars in Ursa Major; Herzsprung added 8 to this group, of which Sirius was the most important as both its parallax and radial velocity were known. Rasmuson uses 28 stars to find the vertex $A = 308°$, $D = -40°$, and a speed of 19 kilometers per second. The sun is within the limits of this group, so the parallaxes may vary widely.

In the latter part of the century, Boss and Kapteyn computed apices from proper motions depending largely on Bradley stars. These agreed in right ascen-

[10] A.N., 16, 65–96.
[11] L.O.B., 229.
[12] A.J., 26, 31–36.

sion but differed by 15° in declination; this led Kapteyn to investigate the cause of the disagreement. At the St. Louis Congress of Arts and Sciences,[13] he presented an address in which he showed that the stellar motions were not at random, but showed preference for two directions; one toward A = 85°, D = −11° and the other toward A = 260°, D = −28°. He suggested that there were two streams of stars moving in different directions and commingling; in each stream we can assume that the motions of the individual stars are at random. This two-stream or two-drift hypothesis at once took a prominent place in discussions of the stellar system. An alternative interpretation was offered by Schwarzschild: if the frequency of velocities in any direction be represented by a vector, the surface outlined would be an ellipsoid, with major axis in the direction of the vertices of preferential motion.

Eddington, using the stars from Grombridge, confirmed Kapteyn's results; so did Dyson, using the stars in the Cape Astrographic and also the stars in Carrington's Catalogue.

Kapteyn said that we have two new weapons in the twentieth century—photography, which dreads no numbers, and spectroscopy, which does not care for distances.

Campbell in 1900, using provisional values of the radial velocities for 280 stars, found the apex A = 277°.5, D = 20°, and the solar velocity V = 19.9 km/sec. The solar motion is obtained directly from these radial velocities. In his volume "Stellar Motions" Campbell gives a result from 1,047 radial velocities; A = 272°, D = 27°.4, V = 17.8 km/sec. When he classifies these radial velocities according to the type of spectra, he finds an increase in velocity in going from the earlier spectral type to the later:

O and B	9.0 km/sec
A	9.9 "
F	13.9 "
G and K	15.1 "
M	16.5 "

In 1928, Campbell and Moore[14] published and discussed 2,149 radial velocities of stars brighter than magnitude 5.5. Again their values are nearly the same: A = 270°.6, D = 29°.2 and V = 19.6 km/sec. Again they note that the average residual velocity of the star increases with the spectral class:

B	8.7 km/sec
A	9.9 "
F	12.5 "
G	14.8 "
K	15.3 "
M	16.1 "

Most of these stars are giants, and a few dwarfs occur only in classes F and K. When the solar motion was determined for each spectral class, the groups B and M gave a larger value—22 km/sec—than those from A to K, which averaged 18.7 km/sec.

With the increasing material available, we find the space motions of the stars under investigation in the decade from 1920 to 1930. Thus Strömberg,[15] in considering the distribution of velocities, found 1,300 stars whose proper motions, parallaxes and radial velocities had been determined so that their space motions relative to the sun were known. He found that the solar motion depended on the spectral type and absolute magnitude; that dwarf stars gave a larger solar motion than giants, and high velocity stars than low velocity stars. A study of peculiar velocities was made after correcting these space motions for a solar motion of 20 km/sec toward the apex, A = 270°, D = 30°. He states that the giant stars of types F to M form a single group or stream with approximately ellipsoidal distribution. In addition about 20 per cent. have a stream motion coinciding with the Taurus moving cluster; these are scattered all over the sky. "There is marked asymmetry in the distribution of the velocities around the most frequent velocity vector"; and stars of high velocity move toward the region limited by galactic longitudes 134° to 334°.

Studying this asymmetry in a second paper, Strömberg used a quantity $H = m + 5 \log \mu$ as a basis for his division into groups. He found that the group motion changed continuously with velocity dispersion along an axis in the direction $\alpha = 309°.8$, $\delta = 57°.1$; it varied from 9.0 km/sec for Cepheids of long period to 300 km/sec for fast-moving objects, globular clusters and spiral nebulae. The galactic latitude of this axis is 9°, showing the prevalence of motions parallel to the Milky Way.

Wilson and Raymond[16] made a comprehensive study of the motions of 4,233 stars, three times the number used by Strömberg and twice the number used by Campbell and Moore. It was necessary to use statistical parallaxes for only 10 per cent. of the material. Using a provisional apex—275°, 30°—and a solar velocity of 19 km/sec, the space velocities were corrected for the solar motion, and the resulting peculiar velocities were divided into groups with a velocity range of 5 kilometers. For the groups 0 to 25 km/sec, the velocities were random; for the groups 25 to 45 km/sec, Ursa Major and Taurus streaming was superposed on the random motion; for the groups 45 to 65 km/sec, streaming of the giant G, K, M was superposed on the random motion. After we pass 60 km/sec, the values for the apex increase in both right ascension and declination; also the velocity of solar

[13] Congress of Arts and Sciences, 4, 413.

[14] Publ. Lick Obs. 16, Introduction.

[15] A.J., 59, 228; 61, 363.

[16] A.J., 40, 121–142.

motion increases. The values for velocities greater than 250 km/sec are: A = 328°, D = 53° and V = 284 km/sec. It is to be noted that 90 per cent. of these motions can be considered as at random or as random and stream motion combined; only 10 per cent. were asymmetric. The increase of stellar speed with advancing type holds for the main sequence. The low solar speed found for the A group was due to the Ursa Major stars; the small declination of the apex for the F group was due to stars of both streams.

In the last dozen years another result has been obtained from stellar velocities—galactic rotation A term, depending on motion along the galaxy, had been introduced in the equations for precession or solar motion, by some computers in the last century; but it always came out vanishingly small. Theoretical results in this century pointed to such a rotation; certain other results, such as the asymmetry of high velocities, the great solar motion with reference to the globular clusters, the variation of the K term with galactic longitude pointed in the same direction. I believe the first determination from radial velocities was made by Oort;[17] he found the center about which rotation took place was in longitude 326° and the velocity of rotation was 275 km/sec.

Plaskett and Pearce,[18] using proper motions of 881 stars and radial velocities of 849 stars of types O to B7, confirmed the results of Oort; they found $l_0 = 324°$, $V_0 = 275$ km/sec, P = 224000000 years, R = 10000 parsecs.

In a recent paper, Wilson finds similar results; he used Cepheid variables, non-Cepheid c-stars as well as B and O type stars; he adopted a mean galactic absorption of 0.65 mag/kpc. He concluded that the value of V was between 275 and 300 km/sec.

As a rule radial velocities have been preferred to proper motions. The effect of galactic rotation is best seen in distant stars; these have small proper motions, whose accuracy is impaired both by accidental and systematic errors. Van de Kamp and Vyssotsky[19] have used the proper motions of 18,000 stars to determine the solar motion and the galactic rotation. These motions were referred to Boss stars and were corrected for systematic errors due to Newcomb's equinox and precession. The stars were faint stars and their magnitudes extended from 7.5 down to 12.5. They found a value for the solar apex of A = 285°, D = 36°; both values are larger than those usually found for bright stars. For the several spectral classes, their latitudes were systematically greater than those found by Wilson and Raymond.

Values of the solar motion still show dependence on the group used and seem to show variation with spectral type and with magnitude. The results for galactic rotation, either from proper motions or radial velocities, agree quite well.

OBITUARY

HENRY HURD RUSBY

DR. HENRY HURD RUSBY, long an outstanding specialist in the field of pharmacognosy, died on November 18, 1940, at his home in Sarasota, Florida. He was born at Franklin, New Jersey, on April 26, 1855, and until 1938 was a resident of Newark, N. J.

While his early life was that of the average American boy in the rural sections, he even then showed a marked interest in plant life. Fortunately, this natural inclination was stimulated through contact with a teacher in the country school which he attended. Although his formal study of botany was meagre, this was more than compensated by his ability to learn at first hand and from plants themselves rather than from text-books.

The objectives of his botanical explorations were the establishment of new sources of supply for drugs and the search for new drug plants. On the first of the South American journeys from La Paz to Para in 1885–86, supplies of coca leaves, chequen, pichi and cocillana were sought. In addition an extensive study of cinchona cultivation was made and a complete collection of cinchona species acquired. The second journey in 1896 was a general botanical survey of that portion of Venezuela south of the Orinoco. The third of these surveys was in Mexico and was chiefly concerned with the discovery of possible rubber-yielding trees. The fourth and last exploration, in 1919, covered in part the same territory as the first and gave opportunity for comparisons with the conditions of thirty-five years previous. Dr. Rusby was then 64 years of age and had recently recovered from pneumonia. His family and many friends went to the steamer on the blustery March day of his departure. For most of us it was a rather sad occasion with the thought that he would not survive the journey uppermost in our minds. Despite his indomitable will he was forced to return ahead of the main party and continue his studies of the botanical results of the trip in the laboratory rather than in the field.

Dr. Rusby was professor of materia medica at the Columbia University College of Pharmacy from 1888 to 1930. Coincident with that appointment he taught materia medica in the New York University Medical School and the New York Veterinary College for

[17] B.A.N., 120.
[18] M.N., 679–713.
[19] Publ. Leander McCormick Obs., Vol. 7.

several years. With Professor Charles F. Chandler he was instrumental in bringing about the affiliation of the New York College of Pharmacy with Columbia University in 1904, at which time he became dean of the former institution and served as such until 1930.

Dr. Rusby's interest in the field of botany early influenced him to become an active member of the Torrey Botanical Club. He was president of the club from 1905 to 1912, and this association was particularly appropriate because in 1829, Dr. John Torrey was one of the first professors in the then newly organized College of Pharmacy. As a close friend of Dr. Nathaniel L. Britton, Dr. Rusby shared in the founding of the New York Botanical Garden. As one of the incorporators, chairman of the scientific directors and curator of the economic collections, he witnessed the continuous development of that institution.

Aside from his contributions to the literature of taxonomy, education in pharmacy and writings upon other subjects, he was author or co-author of "The National Standard Dispensatory," "Morphology and Histology of Plants," "A Manual of Botany," "Properties and Uses of Drugs," "Essentials of Vegetable Pharmacognosy" and "Jungle Memories."

The honors which were bestowed upon him were richly deserved and came to him without directed effort on his part toward their attainment. He was president of the American Pharmaceutical Association in 1910; one of the organizers of the Conference of Pharmaceutical Faculties, forerunner of the American Association of Colleges of Pharmacy; long a member of the Pharmacy Council, Education Department, New York State; member of the Revision Committees of the Pharmacopoeia of the United States and the National Formulary; Remington Medallist (1923) of the American Pharmaceutical Association; Hanbury Medallist (1929) of the Pharmaceutical Society of Great Britain and recipient of the Fluckiger Medal (1937) of the Society of German Apothecaries.

Possibly the real character of a man is most fully revealed in the personal letters he writes during his lifetime. They are seldom written with any thought of future publication and therefore give one a better appreciation of the man as he actually was than could be had from a biographical sketch. From a close association of over thirty years, it would be possible for me to give my impression of Dr. Rusby as a scientific worker, a preceptor and a friend, but I prefer that he should speak for himself through the following quotations from my file of his letters.

> I can not say too strongly that in my opinion the first and most important consideration is absolute loyalty in adhering to principle. This does not mean stubbornness in having your own way when the decision is against you. It may be necessary to yield in practice but you are not compelled to admit a wrong principle.
>
> Unfortunately honesty frequently does not yield results which are sufficiently immediate to warrant the old adage. Perhaps the dishonest people do win at the expense of the others, yet I would adhere to the honest course to the very end as the ultimate good of humanity depends on that sacrifice and the one object of life is the improvement of human character.

C. W. BALLARD

COLLEGE OF PHARMACY,
COLUMBIA UNIVERSITY

SCIENTIFIC EVENTS

A NEW COURSE IN AIRCRAFT PRODUCTION AT NEW YORK UNIVERSITY

A GRADUATE program in aircraft production, the first to be offered in an American university, will open on February 4 at the College of Engineering of New York University. The course will be given in the evenings at the Washington Square Center.

Commenting on the problem of aircraft production at this time, Dr. Alexander Klemin, director of the college's Guggenheim School of Aeronautics, stated that it was vital that the aircraft industry should apply the general production principles of the automobile industry in obtaining an ever-increasing supply of aircraft. He said:

> The principles of mass production as evolved through the years by the automobile industry have given us the greatest productive capacity in the world in this field.
>
> The airplane industry must add to its magnificent tradition of research and experimentation by becoming production minded, and utilize fully all the production knowledge of the automobile industry.
>
> But in the long run the main responsibility for airplane production must be with the aviation people themselves, no matter how active the automobile industry may be in supplying parts, for while airplane production is indeed changing from what might be called odd-lot custom building to mass production it is a fallacy to believe that airplane production is exactly like auto production. The automobile industry, for example, does not, in between new models, face the possible hazard of an enemy superiority in equipment making its entire output obsolete overnight.
>
> It is with this belief, therefore, that aircraft men must face the problem themselves and receive special training. To this end we have worked out with the cooperation of men versed in general and automobile production, and others from the leading aircraft manufacturers, this course in the principles and practice of aircraft production.

The course will cover organization for control of

production, production planning and control, straight-line production, materials used in airplane production, machinery used in airplane production, processes used in airplane production, materials used in aircraft engine production, machinery used in airplane engine production, processes used in aircraft engine production, purchase of materials, analysis of costs in production, production planning in present-day aircraft factories and engineering organization in present-day aircraft factories.

Administrative and aeronautical engineering departments and outside lecturers from industry will assist Dr. L. P. Alford, chairman of the administrative engineering department, in presenting the course material. Visiting lecturers, widely known in aviation circles, will be E. V. Farrar, Wright Aeronautical Corporation; Guy A. Luburg, Brewster Aeronautical Corporation, and George F. Titterton, Grumman Aircraft Engineering Corporation.

The course will be given in the evenings so as to be available to graduate engineers already employed in industry. It will also be open to men who are not already graduate engineers provided that the training received in the course is likely to serve the purposes of increased aircraft production.

FELLOWSHIPS AND SCHOLARSHIPS IN ENGINEERING AT CORNELL UNIVERSITY

To assist the National Defense program and industry in general in providing urgently needed engineers, Cornell University has initiated a nation-wide inquiry for fifty of America's best qualified secondary school seniors to be trained as engineers. They will be awarded John McMullen Regional Scholarships in Engineering this spring. The scholarships carry variable stipends up to $400 a year throughout a four- or five-year course in the College of Engineering. Application blanks and instructions have been mailed to more than 3,000 principals and head masters throughout the United States.

The John McMullen Fund, which now amounts approximately to $2,000,000 and is still growing, represents the income from a bequest of the late John McMullen, of Norwalk, Conn. The annual income from the fund is used, as the donor specified, "for the education of young men as engineers." There are now 171 McMullen regional scholars in residence, as well as a number of McMullen undergraduate scholars and McMullen graduate scholars. More than 800 young men have received aid from this fund since its foundation, and the total amount available for scholarships in the College of Engineering is now more than $100,000 each year.

Awards to secondary school seniors will be made in fifteen districts including all states except New York, where other scholarships are available. Some scholarships will be held in reserve, however, and may be awarded to superior students from any state after they have been in residence and have shown their ability in the College of Engineering. The bases of award are character and general ability as well as academic distinction.

Other fellowships to be awarded are the Elon Huntington Hooker fellowship in hydraulics at $510, the Charles Bull Earle memorial fellowship in electrical engineering at $400, and several others in various branches of engineering at $400 and $200, with free tuition.

Applications must be filed with the dean of the College of Engineering by April 1, in order that there may be time for thorough investigation by the regional alumni committees who cooperate in the selection.

Fields of study open to students in the college include mechanical, civil, electrical and chemical engineering, and administrative engineering in mechanical, civil or electrical engineering.

THE AMERICAN MUSEUM–SINCLAIR DINOSAUR EXPEDITION

DR. BARNUM BROWN, leader of the American Museum-Sinclair Dinosaur Expedition of 1940, has returned to the American Museum from a four-months expedition to Texas. The other members of the expedition were Dr. Erich M. Schlaikjer, instructor of geology and paleontology at Brooklyn College, and Roland T. Bird, of the American Museum.

Dinosaur remains were first noted in the Big Bend area by Dr. Brown in 1906 and several specimens were found there in the summer of 1939 by Dr. Schlaikjer during a reconnaissance for the American Museum. This year's expedition to the Big Bend area and central Texas collected 44,000 pounds of important specimens that are said to open up a new horizon in the knowledge of dinosaur life, especially of the sauropod type of dinosaur.

Dr. Brown states that this is one of the most interesting collections of dinosaur remains so far discovered because it will make it possible to clarify the geology of the region and give a more complete picture of the prehistoric life in North America during the Age of Reptiles. The discoveries show that the sauropod dinosaurs in this southern region persisted for millions of years after they had disappeared from what is now the northern United States where their remains are better known. Evidence shows that this was due to the fact that climatic conditions favorable to the sauropod life continued in the south long after Wyoming and Montana had become the graveyard of prehistoric creatures of similar type.

Parts of eleven animals, including sauropods, horned and duck-billed dinosaurs and some of low plates spe-

cies were obtained. One of the interesting specimens is a single neck vertebra, larger than anything in the American Museum collection and probably the largest of record. This bone was part of a great sauropod resembling Brontosaurus.

Another find was the skull, teeth and plates of a crocodile having teeth three inches long and one inch in diameter, a crocodile that lived in Upper Cretaceous times some 70,000,000 years ago, and which in size was as large as some of the dinosaurs.

Two distinct kinds of horned dinosaurs are represented in the collection, also a complete skull of a low-plated dinosaur resembling Palaeoscincus (one of the heavily armored types of dinosaurs). Duck-billed dinosaur remains were most numerous and they too differed from the better known northern forms mainly in being slender, longer-legged types.

One of the primary objects of Dr. Brown's forty-five years of dinosaur hunting has been to find the footprints of a sauropod. While Dr. Brown and Dr. Schlaikjer were working in the Big Bend area, Mr. Bird uncovered a trail of these tracks eighty miles southwest of Fort Worth—the first to be recorded—and with the assistance of WPA workers excavated a section of the trail—a slab of limestone twenty-nine feet in length and seven feet wide bearing the impressions of the four feet of a Brontosaurus.

Besides the dinosaur specimens and tracks the collection includes associated fossil plants and shells; large palm leaves; oysters that measure fourteen inches in length and six inches in width, and huge clam shells—one of which measures forty inches in diameter.

WORK OF THE FIELD MUSEUM OF NATURAL HISTORY DURING 1940

MAJOR CLIFFORD C. GREGG, director of the Field Museum of Natural History, has issued a report for the year just closed, summarizing the activities of the institution. He states that the opening of a large and important exhibition hall, the Hall of Babylonian Archeology, constituted the major accomplishment of the museum. This hall represents one of the most ambitious projects in the reconstruction of the life and history of a long past epoch undertaken by the museum. Its preparation was carried out under the supervision of Richard A. Martin, curator of Near Eastern archeology.

In addition to the new hall, many other exhibits were installed in all departments during the year. Among these are habitat groups of kiwi, red grouse and fur seals, a diorama illustrating the spring flora of the Chicago area, a series of large mural paintings by Julius Moessel telling the story of the world's food plants and a new type of analytical-biological exhibit graphically answering the question "What Is a Bird?"

While the exact figure must await a tally of attendance at closing time on December 31, the number of visitors to the museum in 1940 would exceed the total of the preceding year, which was 1,410,454. It was pointed out also that many additional hundreds of thousands were reached by such extra-mural activities as those conducted for school children by two especially endowed units of the museum organization—the N. W. Harris Public School Extension and the James Nelson and Anna Louise Raymond Foundation for Public School and Children's Lectures; and many others by lectures for adults, guide-lecture tours, "layman lectures," a series of radio broadcasts, a series of television programs, publications, etc.

Field work was conducted by a number of museum expeditions. The largest scale operations were those of the Magellanic Expedition, which had begun work in 1939, and continued during the first half of 1940. Under the leadership of Dr. Wilfred H. Osgood, chief curator of zoology, this expedition made a biological survey of parts of southern Peru, Bolivia, Argentina, Chile, the shores of the Straits of Magellan and the island of Tierra del Fuego at the southernmost tip of the South American continent. Accompanying Dr. Osgood were Colin Campbell Sanborn, curator of mammals; Karl P. Schmidt, curator of amphibians and reptiles, and John Schmidt, field assistant.

During the early months of the year the Leon Mandel Caribbean Expedition collected birds, mammals, fishes and reptiles among out-of-the-way islands and keys. The expedition was led by Leon Mandel, of Chicago, aboard his yacht, *The Buccaneer*. Museum collectors in the party were Rudyerd Boulton, curator of birds, and D. Dwight Davis, assistant curator of anatomy and osteology.

The department of botany continued its intensive project of making a comprehensive collection of the flora of Guatemala. Paul C. Standley, curator of the herbarium, and Dr. Julian A. Steyermark, assistant curator, conducted expeditions for this purpose.

A botanical expedition to Mexico and the southwestern United States, begun in 1939 by Dr. Francis Drouet, curator of cryptogamic botany, and Donald Richards, of the Hull Botanical Laboratory of the University of Chicago, concluded its work in 1940, returning with a large collection of specimens.

An important collection of the fossil fauna of South Dakota and Nebraska was obtained by an expedition led by Paul O. McGrew, of the Division of Paleontology. Birds of Yucatan were collected by Melvin Traylor, Jr., and E. Wyllys Andrews, friends of the museum who sponsored and conducted their own expedition. An expedition to collect specimens relating to structural and dynamic geology was conducted in Wyoming, Colorado and South Dakota, and in various

eastern states as well, by Sharat K. Roy, curator of geology, and Henry Herpers, assistant curator of geology. Bryant Mather, assistant curator of mineralogy, conducted a similar expedition in Maryland.

The output of museum publications, both technical and popular, was continued on a large scale by Field Museum Press. The technical publications are distributed internationally among scientific institutions and individual scientists. Notable additions were made to the library's collection of scientific books and pamphlets, now numbering approximately 121,000 volumes.

MEDAL OF HONOR OF THE INSTITUTE OF RADIO ENGINEERS

THE Medal of Honor of the Institute of Radio Engineers for 1941 was awarded to Dr. Alfred N. Goldsmith, New York radio engineer, at the annual convention of the institute at the Hotel Pennsylvania in New York, on the evening of January 10. The award was made for "his contribution to radio research, engineering and commercial development, his leadership in standardization and his unceasing devotion to the establishment and upbuilding of the institute and its 'Proceedings.'" The medal was presented to Dr. Goldsmith by the president of the institute, Professor Frederick E. Terman, of California.

Dr. Goldsmith has been active in the radio field throughout the period of its major growth and development. He has been president of the Institute of Radio Engineers as well as president of the Society of Motion Picture Engineers. He is a fellow of the American Institute of Electrical Engineers, of the Acoustical Society of America, of the Optical Society of America and of other engineering and scientific organizations. He has made numerous inventions in the fields of radio transmission and reception, broadcasting, facsimile, photographic technique, acoustical improvements (including a device for the electrical production of room resonance or reverberation), optics (including an effective method for increasing the depth of field in photography), and in television (including methods of introducing pictured backgrounds electrically into television images, methods of using a number of small cathode-ray tubes to produce a large television image, and methods of producing advanced motion-picture effects in television programs).

Dr. Goldsmith, who studied under the late Professor Pupin at Columbia University, was at one time professor of electrical engineering at the College of the City of New York, a consulting engineer of the General Electric Company and a vice-president of the Radio Corporation of America. He is now active as a consulting engineer. In 1935 he received an honorary degree of doctor of science from Lawrence College, and in 1940 he received a National Pioneer Award for "distinguished achievement in the field of science and invention which has advanced the American standard of living."

SCIENTIFIC NOTES AND NEWS

THE Gold Medal of the American Institute of the City of New York for 1941 has been awarded to Dr. Wendell M. Stanley, member of the Rockefeller Institute for Medical Research at Princeton, N. J. The award is in recognition of his work "for crystallizing the virus of tobacco mosaic, a feat which has opened up new fields of research, given birth to new ideas about the nature of important disease-producing agents, and enlarged the human understanding of life." It will be presented at a dinner at the Hotel Pierre on Thursday evening, February 6. On the same occasion, the annual fellowship of the institute will be given to Harry A. Carpenter, specialist in science for the Rochester Schools, "for his influence on the teaching of science throughout the nation as president, for many years, of the American Science Teachers Association, and for his long and successful devotion to education by radio." Both medal and fellowship awards will be presented by Dr. H. C. Parmelee, president of the institute. Dr. Stanley will be introduced by Dr. Thomas M. Rivers, director of the Hospital of the Rockefeller Institute for Medical Research. Mr. Carpenter will be presented for the fellowship award by Dr. S. R. Powers, of Teachers College, Columbia University. Dr. Stanley will make an address entitled "Some Chemical, Medical and Philosophical Aspects of Viruses." He will show virus-diseased plants and demonstrate some physico-chemical properties of the tobacco mosaic virus.

THE Penrose Gold Medal, which was awarded to Dr. Nelson Horatio Darton, for more than half a century geologist of the U. S. Geological Survey and author of maps, folios and reports, was presented to him on December 27 at the Austin meeting of the Geological Society of America. The address of commendation was made by Professor Douglas Johnson. In reply Dr. Darton stated that he regarded "the award as the highest honor he could receive and that it came from the greatest scientific fellowship in the world." He is one of the half dozen surviving original fellows, dating back to 1888.

DR. D. WAYNE WOOLLEY, fellow of the Rockefeller Institute for Medical Research in New York, on De-

cember 28 was awarded the Lilly Prize of $1,000 and a bronze medal given for exceptional contributions in bacteriology at the convention of the Society of American Bacteriologists held in St. Louis.

DR. PHILIP R. WHITE, associate of the Rockefeller Institute for Medical Research, of the Department of Animal and Plant Pathology, Princeton, N. J., received on December 31 the Stephen Hales Award of the American Society of Plant Physiologists at its meeting held in Philadelphia.

THE King of Thailand has conferred on Dr. Robert L. Pendleton, soil technologist and agriculturist of the Department of Agriculture and Fisheries, the title of commander of the most noble order of the Crown of Thailand. At a meeting on November 6 of the council of the Thailand Research Society, Bangkok, formerly known as the Siam Society, it was voted unanimously to tender congratulations to Dr. Pendleton.

DR. P. BOYSEN JENSEN, professor of plant physiology in the University of Copenhagen, known for his work on plant metabolism and growth substances, has been elected a corresponding member of the American Society of Plant Physiologists.

AT the thirty-ninth annual meeting of the American Anthropological Association, held in Philadelphia on December 29, the following officers were elected: *President,* Elsie Clews Parsons; *First Vice-president,* Earnest A. Hooton (1941); *Second Vice-president,* Wm. Duncan Strong (1941–1942); *Third Vice-president,* Ruth F. Benedict (1941–1943); *Fourth Vice-president,* S. K. Lothrop (1941–1944); *Secretary,* Frederick Eggan; *Treasurer,* Bella Weitzner; *Editor,* Ralph Linton; *Associate Editors,* Melville Jacobs, F. H. H. Roberts, Jr., Harry Shapiro; *Executive Committee,* J. A. Mason, A. V. Kidder, Donald Scott; *Representative to Social Science Research Council* (by vote of 1940 Council to be elected by the Executive Committee); *Representatives to National Research Council,* C. S. Coon, M. W. Stirling, D. S. Davidson (1941–1944); *Representatives to Section H, American Association for the Advancement of Science,* F. M. Setzler, W. D. Wallis (1941); *Representative to the American Council of Learned Societies,* Robert H. Lowie (1941–1944).

Museum News states that the American Association of Botanical Gardens and Arboretums, which was organized at Cleveland on September 25, is an affiliate of the American Institute of Park Executives on practically the same basis as the American Association of Zoological Parks and Aquariums. Officers elected are: Donald Wyman, Arnold Arboretum, *chairman;* Henry T. Skinner, Morris Arboretum, *vice-chairman;* C. E. Godshalk, Morton Arboretum, *secretary;* C. Stuart Gager, Brooklyn Botanic Garden, and H. Teuscher, Montreal Botanic Garden, *directors.* The official publication of the new organization is a section in the magazine *Parks and Recreation.* It began with the December issue and is under the editorship of Mr. Skinner.

AT the annual meeting and banquet of the Torrey Botanical Club, held at the Men's Faculty Club, Columbia University, January 7, the following officers were elected: *President,* John S. Karling, Columbia University; *First Vice-president,* E. B. Matzke, Columbia University; *Second Vice-president,* H. K. Svenson, Brooklyn Botanic Garden; *Editor,* H. W. Rickett, New York Botanical Garden; *Corresponding Secretary,* H. C. Bold, Columbia University; *Recording Secretary,* John W. Thomson, Jr.; *Treasurer,* H. N. Moldenke, New York Botanical Garden; *Business Manager,* Michael Levine, Montefiore Hospital; *Bibliographer,* Mrs. Lazella Schwarten, New York Botanical Garden; *Council Members,* R. C. Benedict, Brooklyn College; Mrs. Helen M. Trelease, J. H. Barnhart, New York Botanical Garden; *Delegate to New York Academy of Sciences,* W. J. Robbins, New York Botanical Garden; *Delegates to the Council of the American Association for the Advancement of Science,* C. S. Gager, Brooklyn Botanic Garden, B. O. Dodge, New York Botanical Garden; *Representative to the Board of Managers of the New York Botanical Garden,* H. A. Gleason.

DR. R. A. FISHER, Galton professor at University College, London, will be visiting professor of experimental-statistics at North Carolina State College during the summer session, June 16 to July 25. Professor Gertrude M. Cox, head of the newly established department of experimental statistics, has invited several other leaders in various fields of applied statistics to go to the college this summer to assist in conducting special courses and conferences.

DR. MAX R. ZELLE has been appointed assistant professor of genetics at Purdue University. He is teaching general genetics and has charge of research in animal genetics in the Experiment Station.

DR. DALLAS B. PHEMISTER, professor and chairman of the department of surgery of the School of Medicine of the University of Chicago, has been designated the first holder of the Thomas D. Jones professorship newly established in honor of the late Thomas Davies Jones, attorney and industrialist, who died in 1930.

DR. R. G. JAAP, of the department of poultry of the Oklahoma Agricultural and Mechanical College, and associate editor of *Poultry Science,* has recently been advanced to the rank of associate professor of poultry husbandry in charge of poultry genetics.

LEONARD A. SALTER, JR., senior agricultural economist in the Division of Land Economics of the Bureau of Agricultural Economics of the Department

of Agriculture, has taken up his work as professor of agricultural economics at the University of Wisconsin.

DR. FRANCIS DROUET has been given a permanent appointment as curator of cryptogamic botany at the Field Museum, Chicago, following his completion of a two-year temporary appointment begun in 1938. During the first two years of his association with the museum, Dr. Drouet has begun reorganization of the collections of cryptogamic plants in the department of botany, and has conducted an expedition to the American Southwest and Mexico.

DR. B. E. DAHLGREN, chief curator, department of botany of the Field Museum, Chicago, has returned to his post at the museum after an extended trip to Brazil.

PROFESSOR EDWIN G. CONKLIN, of Princeton University, will give the fourth annual William Keith Brooks Lecture at Greensboro College, S. C., on March 10. His lecture will be entitled "The Geography of Eggs."

DR. ERNEST E. IRONS, Chicago, delivered on December 6, under the auspices of the Phi Chi fraternity, the annual Charles R. Bardeen Memorial Lecture at the Medical School of the University of Wisconsin. The lecture was entitled "Aspiration Pneumonia: Pathology-Bacteriology-Symptoms."

DR. VIRGIL H. MOON, professor of pathology, Jefferson Medical College, Philadelphia, on December 20 gave the annual Gross Lecture of the Pathological Society of Philadelphia. It was entitled "Pathology and Vascular Dynamics of Shock."

DR. GEORGE W. BACHMAN, director of the School of Tropical Medicine of the University of Puerto Rico, which is under the auspices of Columbia University, gave on December 18 an address at the Long Island College of Medicine on "Tropical Medicine: Its Historical Background and Its Importance in National Defense."

THE seventieth annual meeting of the American Public Health Association will be held from October 14 to 17 at Atlantic City, N. J. Headquarters will be the Convention Hall. Residence headquarters will be the Hotel Traymore. The sixty-ninth annual meeting held in Detroit in October attracted an attendance of more than thirty-one hundred, from all parts of the United States and also from Canada, Cuba and Mexico. A New Jersey committee responsible for entertainment, inspection trips and other local aspects of the meeting is being formed under the direction of Dr. S. L. Salasin, health officer of Atlantic City. Among the related organizations meeting with the association are the American School Health Association, the International Society of Medical Health Officers, the Association of Women in Public Health, the Conference of State Sanitary Engineers, the Conference of Municipal Public Health Engineers and the Conference of State Provincial Public Health Laboratory Directors.

DR. CHARLES L. PARSONS, secretary and general manager of the American Chemical Society, announces that the society has acquired the property at the southwest corner of Sixteenth and M Streets, Northwest, as a national home. The purchase is described as an important step in the development of Washington as a major center of activity in science, education and related fields. Willard H. Dow, president of the Dow Chemical Company, Midland, Mich., was chairman of a special committee of the directors that recommended the acquisition. Other members of the committee were: Dr. Leason H. Adams, of the Geophysical Laboratory, Washington; Dr. Gustavus J. Esselen, of Boston, and H. C. Morris, of Washington. "The property," it is said, "is in one of the most desirable locations in Washington."

DR. GEORGE B. CRESSEY, chairman of the department of geology and geography of Syracuse University, writes: "Before the National Geological Survey of China was obliged to leave Peking some years ago, work had been completed on a relief model of the entire country. This provides the best available representation of the topography of this corner of Asia. The plaster cast measures 23″ × 32″, on a scale of 1:7,500,000 with 15 times vertical exaggeration. The area includes all of the Tibetan Highlands, portions of India and the Soviet Union, the Japanese Islands, detailed depths well into the ocean, as well as the configuration of all China. The topography is exceptionally good. The model is lettered in English. The department of geology and geography at Syracuse University has just secured a cast from private sources in Peking. Due to the favorable exchange, the cost is but $20 plus freight. Dr. Cressey will be glad to place interested institutions in touch with the source of supply. Universities and museums which display models of other parts of the world should take advantage of this opportunity at an early date."

A CORRESPONDENT of the London *Times* states that by German decree the University of Leyden and the Technical High School at Delft have been closed owing to the "generally anti-German attitude of the undergraduates, and sabotage of the anti-Jewish measures." All professors of the Faculty of Laws of the University of Utrecht have been sent to concentration camps in Germany, while several professors of the Catholic University at Nijmegen, and of the Commercial High School at Rotterdam, have been arrested because of their loyalty to the House of Orange and openly admitted preference for a democratic system of government. A number of students at all these institutions have been arrested, fined or sent to concentration camps.

DISCUSSION

A CHINESE INSECTICIDAL PLANT, TRIPTERYGIUM WILFORDII, INTRODUCED INTO THE UNITED STATES

Tripterygium Wilfordii, Hook f., called lei kung teng,[1] "Thunder God vine," by the Chinese, is a perennial twining vine belonging to the family Celastraceae with foliage and manner of growth very much like that of our native North American bittersweet, *Celastrus scandens* L. The fruit of *Tripterygium,* however, differs from the bright orange and scarlet clusters which the bittersweet vine bears in profusion in autumn; it is dry, indehiscent, yellowish green or brownish in color, 1.5–2 cm long and 7–10 cm wide, with 3 wings, running lengthwise.

Tripterygium Wilfordii is cultivated rather widely in several Chinese provinces on the south side of the Yangtze River, especially in Chekiang Province. The Chinese market gardeners have for a long time made use of the powdered roots of this plant as an insecticide to kill insects which eat the leaves of vegetables such as cabbage, cucumbers, carrots, etc.

About ten years ago lei kung teng suddenly came into prominence in Chekiang Province because of a dispute regarding the damage to valuable, highly productive valley lands caused by the wash from the nearby hills incident to heavy rains following the harvest of the Tripterygium roots, an operation which leaves the soil loose and easily washed away.[2] The land owners in the fertile valleys asked that the culture of lei kung teng be forbidden, but this quickly provoked the active opposition of the vegetable growers who said they could not grow their crops without using the powdered roots of this plant to kill noxious insects. Entomologists and other experts were sent to investigate the matter, and, in consequence about a dozen important papers and nearly as many more brief notes[3] have been published by Chinese experts since 1931 on *Tripterygium Wilfordii* and its insecticidal use. Some of these reports give in detail proofs beyond question of the insecticidal value, as a stomach poison, of the lei kung teng powder.

[1] Written *lei kung t'êng* in the Wade system of romanization.

[2] Erosion damage so caused in central Chekiang Province is discussed in detail by Lü Chin-lo, cited below in footnote 3 (c).

[3] The more important papers are: (a) Ch'ên T'ung-su, in *Chekiang Reconstr. Monthly,* 5: 74–78, 1931; (b) Lin, Hsiung-hsiang, in *Jour. Agr. Assoc. China,* No. 100, 48–73, ills., 1932; (c) Lü Chin-lo, in *Entom. and Phytopath.,* 1: 256–258, 1933; (d) Ch'ên T'ung-su, in *Jour. Agr. Assoc. China,* No. 118: 67–74, ills., 1933; (e) Yen Chin-lan (Nien, C. L.), in *Jour. Agr. Assoc. China,* No. 125: 79–82, 1934; (f) Chou Ming-tsan, Huang, Shiu-lun and Hsü Yü-fên, in *Chedah Agr. Quart.,* 1: 3–56, ills., 1937; (g) Huang Shui-lun, in *Bull.* 5, Kwangsi Agric. Exp. Sta., 2 pp. 1939. All in Chinese except (g)

In the course of an investigation of Chinese economic plants, translations of these articles were made for the Division of Plant Exploration and Introduction by the Chinese translator, Mr. Michael J. Hagerty, working under the direct supervision of the senior author. Impressed by facts brought to light in these Chinese reports, a trained Chinese plantsman was sent in the autumn of 1935 to Chekiang Province, where this insecticidal plant is grown on a large scale. There he secured several thousand cuttings which arrived in Washington in good condition and grew very well at the U. S. Plant Introduction Garden of the Division of Plant Exploration and Introduction at Glenn Dale, Md.

Root powder of *Tripterygium Wilfordii* sent from China in the autumn of 1935 was given a tentative test in the Division of Control Investigations, Bureau of Entomology and Plant Quarantine, and was found to have little or no value as a contact insecticide. Another small importation of root-powder was made from China, and with it a second test was made by the Division of Control Investigations in the spring of 1936, this time using the root powder as a contact and a stomach poison against the larvae of the silkworm, *Bombyx mori* (L.); eastern tent caterpillar, *Malacosoma americana* (F.); southern armyworm, *Prodenia eridania* (Cram.); and Colorado potato beetle, *Leptinotarsa decemlineata* (Say.). These insects were not affected by contact, but the silkworm, eastern tent caterpillar and the potato beetle larvae were deterred from feeding on leaves dusted with the powdered plant material. The silkworm and potato beetle larvae that fed on the dusted leaves were affected and died after having taken a sufficient dose. The southern armyworm was not deterred from feeding on dusted leaves and was not affected by the dust. This last batch of powders tested was, however, at least six months old when used, and the Chinese insist that the insecticidal value of this powder declines steadily and is entirely lost after one year's storage; therefore it is probable that the powder tested in April, 1936, had already lost much of its toxic power.

In view of the indecisive nature of these preliminary tests of more or less deteriorated powders, it was decided to make further tests as soon as freshly prepared powder could be obtained from the plants growing at the Plant Introduction Garden at Glenn Dale, Maryland. Such root powder was secured in September and October, 1939, from vigorous plants that had made four years' growth.

The material was very toxic to first instar larvae of the diamondback moth, *Plutella maculipennis* (Curt.) and the imported cabbage worm, *Pieris rapae* L. The material caused relatively low mortalities and

in some instances practically none on first instar larvae of the southern armyworm, *Prodenia eridania* (Cram.), second and larger instars of the melonworm, *Diaphania hyalinata* L., and large larvae of the southern beet webworm, *Pachyzancla bipunctalis* (F.). Alcoholic extracts gave slightly better results. The material was very repellent to small larvae which attack Cruciferae but was much less effective than derris on larger ones.

When tested against the larvae of the codling moth, *Carpocapsa pomonella* (L.), by the apple plug method the root powder gave about 60 per cent. clean fruit when used at the rate of two pounds per fifty gallons of solution. An alcoholic extract of the fresh root when used at the rate of two pounds extractives per fifty gallons solution gave 90 per cent. clean fruit. The results against the codling moth larvae have been deemed of sufficient interest to warrant a detailed chemical study of the plant extractive. Such a study is now under way, and the results of the toxicity of the various fractions of the extractive to the insect will be published soon elsewhere.

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PROPOSED NAMES FOR THE FOLLICLE-STIMULATING AND INTERSTITIAL CELL-STIMULATING HORMONES OF THE ANTERIOR LOBE OF THE PITUITARY BODY

DESPITE the widespread use of the cumbrous terms, follicle-stimulating hormone and interstitial cell-stimulating hormone, no investigator has proposed simple etymologically justified names as badly needed substitutes. We should like to propose names which we hope either will be accepted by other investigators or will lead to the coinage of names which will receive general approval.

As a common suffix of both hormones, the term "kentrin" (from *κεντρίζω*, to goad, stimulate) seems suitable. An apt prefix for the follicle-stimulating hormone is furnished by the word *θύλᾰκος*, bag, sack, —a word which Aristotle used to describe the sack in which the eggs of the tunny are enveloped. Therefore, "thylakentrin" is suggested as the name of the follicle-stimulating hormone. This hormone also stimulates or maintains the germinal epithelium of the testis. The name "thylakentrin" also suggests an action on the male gonad since *θυλάκη* is the Greek noun for scrotum.

"Metakentrin" (*μετά*, among, between, and *κεντρίζω* to goad, stimulate) appears to be a suitable name for the interstitial cell-stimulating hormone which has been isolated as a pure substance.[1] This name could refer to stimulation or maintenance of the interstitial cells of either the ovary or the testis.

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THE ENCYCLOPEDIA OF CHEMICAL REACTIONS

A DISCUSSION of this proposed work of reference was printed in SCIENCE for June 15, 1934 (Vol. 79, p. 541). As a result of that article, together with other news reports of a like nature, many chemists volunteered their services, to assist in abstracting chemical reactions for the Encyclopedia.

Up to the present there are twenty-three abstractors, who are either actively engaged with abstracting or have contributed a considerable volume of reactions to the E. C. R. In addition to these, twenty-five other chemists have signified a willingness to assist in the work as soon as a publisher has been secured and the prospects have become more promising for bringing the work into print. This has now been realized. The Chemical Publishing Company, Inc., of New York City, have agreed to sponsor the publication of the E. C. R. and authorizes me to say that any one wishing to join our list of abstractors, will for a small contribution of his time, receive permanent recognition on the Board of Editors, besides enjoying the satisfaction of having helped in compiling a much needed work. The E. C. R. has been called "an indispensable reference work."

The abstracting of eighteen chemical journals is complete to about 1936. The abstracting of twelve others has been begun. Most of the journals in the English, Swedish and Czech languages have been covered, but abstracting assignments can still be secured in the remaining ones and especially in the French, German and Japanese journals. Over 6,000 reactions have been typed and are now ready for the press. It is to be hoped that many other chemists will feel inclined to give some assistance to this "monumental work."

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ANIMAL BEHAVIOR DURING AIR-RAIDS

RECENT months have given observers in Britain an opportunity of obtaining some interesting information relating to the behavior of animals under conditions of modern warfare. A survey of such information as has so far been published would seem to indicate that

[1] T. Shedlovsky, A. Rothen, R. O. Greep, H. B. van Dyke and B. F. Chow, SCIENCE, 92: 178, 1940.

the reactions of animals in general may be classed under three heads: (1) species showing alarm; (2) species showing indifference, and (3) species which react with defiance. While at this stage only preliminary results can be given, it seems that within any one species individual animals will react differently each to the other. Thus, among mammals at least, there is considerable evidence to support the claims of those naturalists who regard animals as capable of having definite and distinctive "personalities."

Huxley[1] has recently given some account of the behavior of the animals of London Zoo during air bombardment. Fell[2] has given similar information in regard to wild animals of the east coast of Scotland. News reports have supplied additional information from time to time.[3]

During recent air-raids on London, a young giraffe deserted its house to sleep in the open (thereby catching a chill). One zebra preferred to take shelter in a basement, while another which had been liberated by a bomb blowing down the gate of its enclosure, emerged to wander through Regent's Park. The monkeys were indifferent. Some ruminants ran about. A crane which was also released went out to the London streets. A donkey reacted defiantly and replied to the noises of the bombs by an angry braying of its own.

During a recent air-raid on the east coast of Scotland a flock of black-headed gulls (*Larus ridibundus*) displayed something akin to mass hysteria when a nearby anti-aircraft battery suddenly opened fire in the early hours of the morning. With one accord the whole colony of several hundred rose into the air in a flurry of startled cries and flapping wings. For nearly an hour afterwards they circled round and round before once more resuming their habitual position on the field that they have made their winter quarters. The smaller wild birds contented themselves in uttering subdued twitterings from their perches in the trees and hedgerows. On the other hand, an owl which has taken up residence in the locality behaved in a manner more akin to the attitude of defiance shown by the London donkey. This bird, probably a tawny owl (*Strix a. sylvatica*) gave vent to its feelings during some unusually intense gunfire by a paroxysm of indignant screeches of a most belligerent tenor. He left no doubt that he resented this unseemly incursion upon the progress of his night-work.

There have been several cases reported of dogs becoming conditioned to respond appropriately to the "Alert" and "Raiders Past" signals. Thus, when the warning sirens go one dog "began to howl and put its tail between its legs," while another went straight to the shelter. On the "Raiders Past" signal, these dogs emerged at once from the place of refuge.[3] Mice are generally regarded as being extremely sensitive to loud noises. However, during one raid, the writer had occasion to enter another room in the house, thereby startling a mouse which had been foraging, unperturbed by the "noises off." Perhaps mice, as well as men, become accustomed to the amenities of twentieth-century civilization.

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SOCIETIES AND MEETINGS

THE WESTERN SOCIETY OF NATURALISTS

The thirteenth annual winter meeting of the Western Society of Naturalists was held at the University of California at Los Angeles on December 18, 19 and 20, 1940. Nearly 100 members and guests registered. Prominent on the program were two evening lectures and three symposia. On December 18, Professor H. S. Jennings addressed an informal evening gathering and smoker on the subject, "The Biological Nature of Man." On December 19, following the annual dinner, Professor G. E. MacGinitie, retiring president of the society, delivered an address, illustrated by both slides and motion pictures, on the feeding habits of some mud-flat animals. The symposia were as follows:

December 18 (morning): "Training for Research and Instruction in the Biological Sciences." *Chairman:* President G. E. MacGinitie. *Contributors:* Dr. I. L. Wiggins, Department of Botany, Stanford University; Dr. Vesta Holt, Department of Biology, Chico State Teachers College; Dr. Raymond B. Cowles, Department of Zoology, University of California at Los Angeles; Dr. Jesse A. Bond, Department of Education, University of California at Los Angeles.

December 18 (afternoon): "The Historical Development of the Climax Communities of the Western United States." *Chairman:* Professor Carl Epling, Department of Botany, University of California at Los Angeles. *Contributors:* A. E. Wieslander, U. S. Forestry Service; H. L. Mason, University of California; D. I. Axelrod, fellow, National Research Council, and I. L. Wiggins, Stanford University.

December 19 (morning): "Perspectives in Marine Biology." *Chairman:* Dr. Robert C. Miller, director, California Academy of Sciences. *Contributors:* Dr. Rolf L. Bolin, Hopkins Marine Station, Pacific Grove; Dr. Robert C. Miller; Dr. C. E. ZoBell, Scripps Institution of Oceanography; Dr. E. R. Norris, University of Washington; Dr. H. U. Sverdrup, director, Scripps Institution of Oceanography.

Officers for the year 1941 were elected as follows:

[1] *The Spectator*, London, November 1, 1940.
[2] *The Spectator*, London, November 8, 1940.
[3] *The Manchester Guardian*, and other sources.

President, Dr. Gordon H. Ball, University of California at Los Angeles.
Vice-president, Dr. Herbert W. Graham, Mills College.
Secretary-Treasurer, Dr. Denis L. Fox, Scripps Institution of Oceanography.

Members of the Executive Committee: Dr. Ira L. Wiggins, Stanford University; Dr. H. L. Mason, University of California.

D. L. Fox,
Secretary

REPORTS

REPORT TO CONGRESS OF THE NATIONAL ADVISORY COMMITTEE FOR AERONAUTICS

"SCIENTIFIC research is the most fundamental activity of the Government in connection with the development of America's potential strength in the air," Congress was told on January 13 in the report of the National Advisory Committee for Aeronautics, transmitted by President Roosevelt. It was submitted to him by Dr. Vannevar Bush, president of the Carnegie Institution of Washington, chairman of the committee.

This quotation from the report and the following further quotations have been selected and sent to SCIENCE by Science Service, Washington, D. C.

"No matter how greatly production facilities may be increased, no matter how many pilots may be trained, unless the aircraft that are built for action are at least equal in performance to those of any possible enemy, the whole effort will be largely wasted," the report continues.

Importance of such research has been recognized, for, it is stated:

"The Army and Navy have maintained the closest contact with the committee's laboratories and have taken the fullest advantage of the committee's facilities in the solution of their pressing problems. The Army Air Corps has appointed at the committee's laboratory at Langley Field a liaison officer, and the Navy's liaison officer, having headquarters in Washington, visits Langley Field at regular and frequent intervals.

"The committee has two major research laboratories, one at Langley Field, Va., known as the Langley Memorial Aeronautical Laboratory, and the others at Moffett Field, Calif., known as the Ames Aeronautical Laboratory. The flight research laboratory was the first unit of the Ames Laboratory to get into operation. Other units will be placed in operation as rapidly as their construction is completed.

"Both the Langley Memorial Aeronautical Laboratory and the Ames Aeronautical Laboratory are devoted chiefly to aerodynamics, although the committee has at Langley Field a structures research laboratory, a hydrodynamics research laboratory and a small engine research laboratory. To remedy the deficiency in engine research facilities the Congress by act approved June 26, 1940, authorized the construction of a third major research station for the committee which is to be an aircraft-engine-research laboratory. The site finally selected by the committee under authority of that act is adjoining the municipal airport at Cleveland, Ohio, and the committee is proceeding with its construction. The details of this action are set forth in Part II of this report.

"The committee highly appreciates the support of the President and the Congress in providing these two additional research stations during the past two years. They were indispensable to strengthen research and to accelerate aeronautical progress in the United States. They will prove of great value to the national defense, and it is confidently predicted that their economic value to the nation will more than offset their cost."

Many of the researches are necessarily secret, for, the report states:

"The committee has found it necessary in the national interests to withhold from public distribution the detailed results of its researches. Therefore, until world conditions change, this and succeeding Annual Reports will deal only in general terms with the results accomplished."

Higher speed planes, with greatly increased armor and armament, are viewed as the outstanding trend produced by the European war. Special studies to meet the requirements are being made.

"The demand for increased speed has resulted in the need for much greater horsepower," the report continues. "Whereas pursuit airplanes of a year ago were equipped with engines of 1,000 horsepower, they are now being designed with single engines of 2,000 horsepower. The trends toward increased speed and higher ceiling, toward larger and heavier engines, toward increased armor and armament, necessitate larger and much heavier types of airplanes. This condition has established a definite trend toward higher wing loadings.

"Because of the higher flying speeds demanded by the Army and Navy, the committee has given special study to the important subject of compressibility shock encountered at high speeds. With the speeds now attainable, it is essential that care be taken to design all parts of the airplane structure so as to prevent velocities approaching the speed of sound from occurring at any point. The 500-mile-per-hour wind tunnel at the Committee's Langley Field laboratory has proved of great value in the study of this problem."

Despite war needs, commercial aviation should not be neglected. The committee believes, it says, "that commercial aviation will prove of ever-increasing importance to the United States in promoting international trade and good will, especially in the Western Hemisphere. When the present wars have ended, aviation will have an opportunity to prove its real value to civilization in shortening the distances between nations and in facilitating international trade and commerce. When that day comes, the extension of world trade routes of the air will bring some compensation for the awful destruction wrought and to be wrought by military aviation before peace again prevails."

SPECIAL ARTICLES

LOCALIZATION OF LITHIUM IN TUMOR TISSUE AS A BASIS FOR SLOW NEUTRON THERAPY[1]

THE destructive action of x-rays and fast neutrons on living tissue is known to be due to the action of energetic electrons resulting from the absorption of the x-rays, and of recoil nuclei, especially hydrogen nuclei, which have been projected by neutron impact. The biological action in either case is a result of energy absorption by the tissue from the high-energy, charged particles. With either x-rays or fast neutrons, however, the destructive action occurs throughout the irradiated tissue, and no satisfactory method has been found for localizing the damage, in the case of cancer therapy, to the tumor zone. Very often skin damage sets an upper limit to the dose which can be delivered through the skin to underlying tissue.

Since the passage of slow neutrons through body tissue is not accompanied by the production of energetic recoil protons, there should be little or no resulting damage from this cause. However, if these slow neutrons be introduced into a zone which has been perfused with certain chemical elements such as boron or lithium, or their compounds, nuclear capture reactions will occur which release very energetic particles, and result in the local destruction of tissue.

The foregoing considerations suggest an investigation of the applicability of neutron-boron or neutron-lithium techniques to the localized treatment of tumors. The method would be based on the introduction of boron or lithium compounds into the tumor region and the subsequent irradiation of this region with slow neutrons. The neutron capture reactions would then result in localized damage to the tumor.

Zahl, Cooper and Dunning[2] injected growing mouse sarcomas with various forms of slow neutron-capturing materials. When the whole animal whose tumor was so injected was irradiated with slow neutrons, a significant increase in tumor regression was observed which presumably resulted from the nuclear disintegration products of the capture process.

In connection with this work, however, it was pointed out that the method of direct hypodermic injection of slow neutron-capturing materials into the tumorous area does not seem clinically feasible. The authors suggested that for any future employment of the boron-slow neutron process in tumor therapy, some device other than simple hypodermic injection should be developed for localizing either boron or lithium, or related materials, in malignant tissue.

The possibility of selective localization in malignant tissue of slow neutron-capturing materials through the medium of intravenous injection was suggested by the work of Ludford,[3] Duran-Reynals[4] and others who observed that certain acid dyes, when introduced into the blood stream, would accumulate in greater concentration in tumor tissue than in normal tissue. Since most of such localizing dyes are sodium salts of the azo-sulfonic acid complex, it was hoped that by substituting lithium atoms for the sodium atoms which are normally present in the dye-salt molecule, the dye molecule would act as a vehicle for localizing lithium in the malignant tissue.

Lithium salts[5] of Pontamine Sky Blue 6B, Trypan Blue and carminic acid were prepared and injected intravenously both into mice bearing spontaneous mammary tumors and mice bearing implanted tumors of the Sarcoma 180 strain. After suitable periods following intravenous injection of the dyes, animals were sacrificed and tumor and other tissues removed and analyzed spectroscopically for lithium content.

Since the purpose in capturing the slow neutrons is to make available the nuclear reaction energy for cellular destruction, it is of interest to compare the amounts of energy made available by the addition of boron and lithium to the tissue in various concen-

[1] We wish to express our appreciation to Dr. C. P. Rhoads and Dr. G. Failla for courtesies extended us at Memorial Hospital, and to Professor J. R. Dunning, of Columbia University. Grateful acknowledgment is made to Lucius N. Littauer, who generously supported certain portions of this work.

[2] Paul A. Zahl, Franklin S. Cooper and J. R. Dunning, *Proc. Nat. Acad. Sci.*, 26: 589–598, 1940. Similar *in vitro* work has been reported by P. G. Kruger, *Proc. Nat. Acad. Sci.*, 26: 181–192, 1940.

[3] R. J. Ludford, *Proc. Roy. Soc.* (London). Series B., 104: 493–511, 1929.

[4] F. Duran-Reynals, *Amer. Jour. Cancer*, 35: 98–107, 1939.

[5] Grateful acknowledgment is made to the Dyestuffs Division of the E. I. du Pont de Nemours and Company and to the National Aniline and Chemical Company for the preparation of the lithium salts of their dyes.

trations. Fig. 1 shows the energy absorbed by the tissue as a function of the concentrations of boron, lithium and their active isotopes.[6] The energy, however, does not become zero at zero concentration because there are neutron reactions with some of the elements in normal tissue, especially hydrogen, nitrogen, chlorine and phosphorus. These reactions liberate a considerable amount of energy but much of it is in the form of penetrating gamma-radiation, and only a small fraction of this is absorbed locally. However, the reaction with nitrogen and the radioactive decay of chlorine and phosphorus yield ionizing particles whose energy is completely absorbed at the site of the reaction. The total energy absorbed by the tissue and due to capture of all the slow neutrons by normal tissue constituents is shown by the horizontal line in Fig. 1. The addition of boron or lithium results in a net increase of absorbed energy, only because more energy is made available when a neutron is captured by boron or lithium than when the neutron is captured by one of the elements of the tissue.

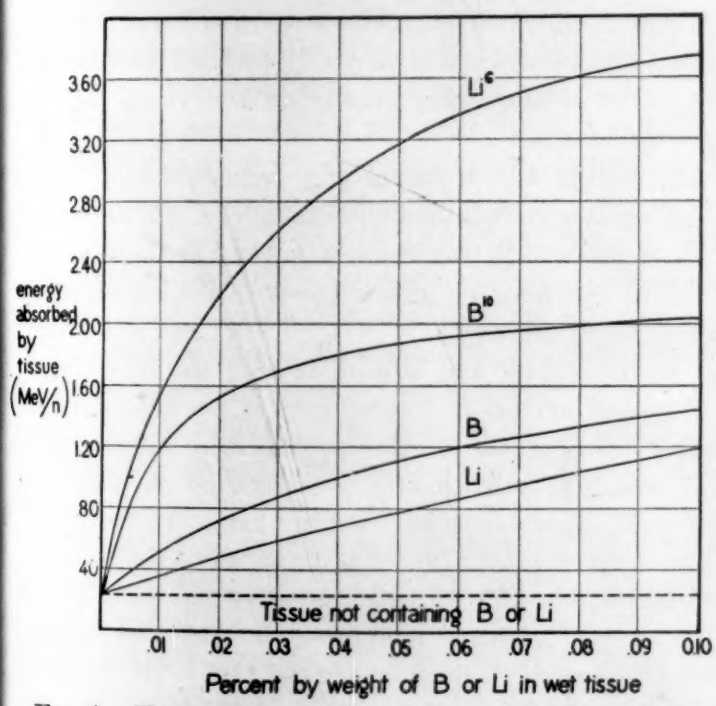

FIG. 1. Energy absorbed by tissue containing varying amounts of boron or lithium or their isotopes. The energy is supplied by slow neutron capture reactions with these elements and with constituents of the tissue.

It is evident from Fig. 1, that increasing the amount of boron or lithium in tissue will continuously increase the total energy absorbed. However, it is not the total energy absorbed but rather the difference in energy between tumor and healthy tissue which determines the optimum treatment condition. This differential dose should be made as large as possible; the absolute amount of the dose can then be adjusted by varying the quantity of slow neutrons administered. In any practical case it would hardly be possible to restrict the added materials entirely to the desired region, *i.e.*, the tumor mass. Rather there will always be boron or lithium in some concentration throughout the region exposed to the slow neutrons. The difference in the radiation dosage supplied to the tumor mass and that to the surrounding tissue, *i.e.*, the dose differential, will therefore depend considerably on the difference in concentration of boron or lithium in the tumor region and in the adjacent tissues. The ratio of these concentrations, which we have called the localization factor, is not, however, the only consideration. The dose differential depends also on the absolute quantity of added material and, in fact, the dose differential passes through a maximum as the quantity of boron or lithium is increased.

In the experimental work done thus far we have attained a localization factor of approximately 2.0 and a maximum concentration of approximately 0.01 per cent. to 0.03 per cent. lithium in the tumor mass. This corresponds to a maximum gain of about 43 per cent. in the radiation dosage of the tumor over that of other tissues in the same mouse. If the isotopes of lithium or boron were available in pure form this advantage could be considerably increased.

The physical and biological considerations here presented apply directly to techniques which might be developed for the treatment of tumors that lie near the surface, thereby permitting the ready penetration of slow neutrons throughout the tumor zone. These considerations also apply to the treatment of deep-seated tumors by a beam of fast neutrons, since they form the basis for an auxiliary technique to utilize the slow neutrons resulting from the slowing down of fast neutrons of the beam. The possibility, not existent with x-rays, of thus securing an increment of ionization localized at a tumor containing boron or lithium provides one of the important reasons for considering the potentialities of fast neutron therapy in conjunction with slow neutron effects.

A detailed study of this problem and an elaboration of the experimental results is being published elsewhere.[7]

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[6] Only the boron isotope of mass 10, *i.e.*, B^{10}, is implicated in the capture of slow neutrons by boron. Since B^{10} atoms comprise only 18.4 per cent. of atoms making up the chemical element boron per unit weight, the "undiluted" B^{10} atoms are 5.5 times as effective as boron in capturing neutrons. Similarly, Li^6 is 12.7 times as effective as lithium. These isotopes are not at the moment available in the quantities necessary for the use indicated, but this condition will not necessarily continue to hold.

[7] Paul A. Zahl and F. S. Cooper, "The Use of Neutrons in Cancer Therapy." *Radiology* (in press), 1941.

CARBONIC ANHYDRASE INACTIVATION AS THE SOURCE OF SULFANILAMIDE "ACIDOSIS"

SULFANILAMIDE produces its desirable bacteriostatic effects and the greater part of its undesirable disturbing effects on acid-base balance,[1] respiration and circulation, through two distinct types of action. The one is exerted through the p-amino group and the other through the opposed, sulfonamide group. Both actions are anti-enzymatic. The one is directed, principally, against catalase and the other against carbonic anhydrase.

The evidence for the anticatalase property of sulfanilamide has already been presented.[2] The evidence for its anti-carbonic anhydrase property is brought forward in the following paragraphs and in a communication by Mann and Keilin[3] which came to our attention as this note was in preparation and which corroborates, in every essential detail, the independently obtained findings reported herewith.

The investigation was suggested by the observation that the degree of tolerance for inhaled CO_2 can be used as a gauge for judging "fitness."[4] Persons optimally fit, as indicated by a minimum incidence of common cold, had been found to make a significantly less excessive respiratory response to inhaled CO_2 than persons with impaired fitness. The fit person appeared to be able to dilute inhaled CO_2 and convert it into non-stimulating[5] bicarbonate more rapidly than the person less fit. The obvious factors of circulatory efficiency, blood volume and CO_2-combining power were considered and attention turned to carbonic anhydrase. This enzyme facilitates, as one of its functions, the conversion of metabolic (or inhaled) CO_2 into bicarbonate.[6]

Markedly decreased tolerance for inhaled CO_2 had been observed during sulfanilamide administration. An arthritic, receiving daily inhalations of 10 per cent. CO_2 in O_2,[7] was able to tolerate 30 liters without difficulty, before beginning and after concluding sulfanilamide therapy. During the therapy he was able to endure only 7.5 liters.

Test was made of the carbonic anhydrase inactivating power of sulfanilamide *in vitro*. A colorimetric method devised by Philpot and Philpot[8] was used in preference to the manometric method used by Mann and Keilin. The colorimetric method measures the time required for conversion of CO_2 into bicarbonate, instead of the converse decomposition of bicarbonate into CO_2. It is significant that both methods led to identical result. In the absence of carbonic anhydrase the average time required for the indicator change marking the endpoint as described by Philpot and Philpot was 68 seconds, while in the presence of 0.0025 cc of laked, defibrinated rabbit blood, 33 seconds was required. The substances tested for inhibitory power were dissolved in the CO_2 solution or added as alcoholic solutions to the reaction mixture in amounts sufficient to give final concentrations of 0.0005 M. Catalysis was completely inhibited by sulfanilamide, acetylaminobenzenesulfonamide, p-toluenesulfonamide and p-caproylaminobenzenesulfonhydroxamide. Sulfapyridine, sulfathiazole, methyl-p-aminophenylsulfone and p-aminobenzoic acid had no effect. The tested compounds were differentiated in their actions against a partially purified preparation of carbonic anhydrase exactly as was found against diluted blood.

Inhibition was apparent only with compounds containing an unsubstituted sulfonamide or sulfonhydroxamide group. It was in no way dependent on possession of the p-amino group known to be essential for therapeutic activity.

Sulfapyridine and sulfathiazole, producing no inactivation of carbonic anhydrase *in vitro*, produce no effects comparable to those produced by sulfanilamide on acid-base balance *in vivo*.[9] The effects produced by sulfanilamide are immediate,[10] requiring for induction only the time necessary for absorption. Both sulfanilamide and sulfocyanate (first shown to be an inhibitor of carbonic anhydrase, *in vitro* and *in vivo*, by Davenport[11]), when given to rabbits in amounts sufficient to give concentrations in the blood equal to or higher than those effecting carbonic anhydrase inactivation *in vitro*, cause the respiratory distress and lengthening of the warming time[12] which would be anticipated to follow carbonic anhydrase inactivation *in vivo*. Loss of appetite is induced, possibly because of a lessened capacity for secreting gastric acid, which can be produced in optimum quantity only when the

[1] A. F. Hartmann, A. M. Perley and H. L. Barnett, *Jour. Clin. Invest.*, 17: 465, 1938.

[2] A. Locke, E. R. Main and R. R. Mellon, SCIENCE, 88: 620, 1938; *Jour. Immunol.*, 36: 183, 1939; E. R. Main, L. E. Shinn and R. R. Mellon, *Proc. Soc. Exp. Biol. and Med.*, 39: 272, 1938.

[3] T. Mann and D. Keilin, *Nature*, 146: 164, 1940.

[4] A. Locke, *Jour. Immunol.*, 39, 1940.

[5] O. Bang, O. Boje and M. Nielson, *Skand. Arch. Physiol.*, Suppl., 10: 1, 1936.

[6] N. U. Meldrum and F. J. W. Roughton, *Jour. Physiol.*, 80: 113, 1933.

[7] A. Locke and M. A. Cohen, *Proc. Soc. Exp. Biol. and Med.*, 43: 611, 1940.

[8] F. J. Philpot and J. St. L. Philpot, *Biochem. Jour.*, 30: 2190, 1936.

[9] P. H. Long, J. W. Haviland, L. B. Edwards and E. A. Bliss, *Jour. Am. Med. Assn.*, 115: 364, 1940.

[10] W. W. Beckman, E. C. Rossmeisl, R. B. Pettingill and W. Bauer, *Jour. Clin. Invest.*, 19: 635, 1940.

[11] H. W. Davenport, *Am. Jour. Physiol.*, 129: 505, 1940.

[12] A. Locke, *Jour. Immunol.*, 36: 159, 1939.

carbonic anhydrase of the parietal cells can function unrestricted by inactivating agents.[13] Carbonic anhydrase injection, into dogs, is reported to produce a rise in alveolar CO_2,[14] indicating increased tolerance.

Fuller, Colebrook and Maxted[15] find that the growth of most group A hemolytic streptococci in human blood is favored by increase in CO_2 and retarded by decrease. In the blood stream, inactivation of carbonic anhydrase would tend to retard conversion of metabolically produced CO_2 into bicarbonate—an action possibly favoring growth and counteracting bacteriostasis. Bicarbonate is reported by Pappenheimer and Hottle[16] to be no substitute for CO_2 for the maintenance of optimum growth. The possession by sulfanilamide of an unmodified sulfonamide grouping capable of producing inactivation of carbonic anhydrase may, therefore, be a source not only of increased toxicity but also of lowered bacteriostatic effectiveness.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

REUNION OF STUMPS OF SMALL NERVES BY TUBULATION INSTEAD OF SUTURE[1]

IN the course of extensive experiments with peripheral nerves of amphibians,[2] recently extended to rats,[3] a method of nerve union has been perfected which, owing to its adequacy and wide applicability, deserves to be placed on record. The problem is to appose closely the cut surface of a proximal nerve stump, as the source of regenerating fibers, to the cut surface of a distal stump, as the channel into which the fibers are to be routed. Apposition by ordinary suturing can never be precise enough to prevent masses of fibers from escaping into the surroundings and straying off to uncontrollable destinations. Moreover, when we are dealing with nerves of only a fraction of a millimeter in diameter, neat suturing becomes a mechanical impossibility. Both difficulties can be met by tubulating the nerve ends with a tightly fitting cuff of fresh artery.[4]

A fragment of artery slightly narrower than the width of the nerves to be united is chosen, squeezed free of blood and immersed in Ringer's solution. All further manipulations take place in this solution. For instruments we use two pairs of hard steel (watchmaker's) forceps ground down until the ends have become very slender and sharp-pointed. The steps of the operation are illustrated in the accompanying figures. (1) With forceps F pull artery A over closed forceps G; artery becomes greatly dilated. (2) Open forceps G slightly and grasp perineurium of nerve stump NP. (3) With forceps F strip artery from G and pull half-way over NP. (4) Withdraw G. (5) Insert F into empty end of artery and open prongs slightly; introduce nerve stump ND into the opening, until the two stumps meet (some additional

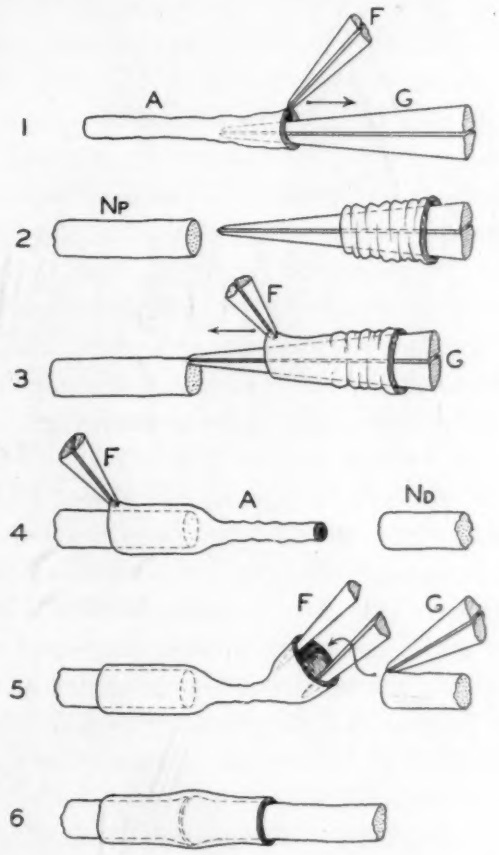

FIG. 1

pressure, flanging the ends, is advisable). (6) Stretch the arterial cuff until it fits snugly.

Enough slack should be allowed to the nerve stumps to insure apposition without stress. After sucking and blotting the excess Ringer's solution from the wound, clotting occurs rapidly. The arterial cuff, firstly, provides a firm link between the nerve ends and, secondly, prevents the formation of a neuroma

[13] Davenport, *op. cit.*
[14] F. Schmitt, *Deut. Arch. klin. Med.*, 134: 300, 1939.
[15] A. T. Fuller, L. Colebrook and W. R. Maxted, *Jour. Path. Bact.*, 48: 443, 1939.
[1] Research aided by the Dr. Wallace C. and Clara A. Abbott Memorial Fund of the University of Chicago.
[2] Paul Weiss, *Biol. Rev.*, 11: 494, 1936.
[3] R. W. Sperry, *Jour. Comp. Neurol.*, 73: 1940.
[4] Tubes filled with various media have been used by surgeons to bridge nerve defects. In the present note tubulation is introduced in a different capacity and on a different order of magnitude.
[16] A. M. Pappenheimer, Jr. and G. A. Hottle, *Proc. Soc. Exp. Biol. and Med.*, 44: 645, 1940.

and the uncontrollable escape of fibers. It is gradually transformed into perineural connective tissue and after several months can no longer be identified. Regenerating fibers traverse the wound in straight parallel courses instead of in the usual confusion following nerve suture.

It has recently been described[5] that good binding between severed nerve trunks can be obtained by applying clotting blood plasma to the apposed cut ends, and that regenerating fibers under these conditions take fairly straight courses in crossing the scar.[6] Whether this method provides the experimenter with as definite an insurance against undesirable stray fibers as tubulation does, remains to be seen.

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A METHOD FOR DETERMINING AND SPECIFYING LOCALITY BY COLLECTORS

WHILE engaged in studying the flora of Maryland the author devised a system for determining and specifying locality which may be of interest to collectors. The system employs the topographical maps published by the United States Geological Survey which are scaled one inch to the mile. These quadrangle maps are already divided by the coordinates of longitude and latitude into nine nearly equal and approximately rectangular divisions. The longitudinal meridians, of course, converge to the north so that the northern boundary of the quadrangle and the northern boundary of every primary division is, in each case, slightly smaller than the opposite or southern boundary. The nine primary divisions of each quadrangle are numbered .1 to .9 counting from left to right: top row, .1, .2, .3; middle row, .4, .5, .6, and bottom row, .7, .8, .9.

A transparent celluloid over-lay is cut the size of an average primary division for the area to be studied. Since no over-lay can be made to fit all the quadrangular divisions for an area as large as the United States, due to the northward convergence of the meridians of longitude, it is necessary to take the average primary division in a given area as the size of the over-lay to be used.

The over-lay may be prepared from either of two kinds of celluloid: (a) with one side frosted so that it may be ruled with India ink, or, (b) with both sides smooth so that lines may be etched or cut into one side and subsequently filled with colored wax or India ink. This over-lay is divided by coordinately ruled lines into nine equal and approximately rectangular divisions each of which represents a secondary division of the quadrangle. These secondary divisions are numbered .01 to .09, and in the manner indicated above for the primary divisions. Each secondary division is, in a similar way, divided into nine tertiary rectangles and numbered .001 to .009. Finally, each tertiary subdivision is divided into nine rectangles which are numbered .0001 to .0009. Thus, the preparation of the over-lay in the manner indicated provides four sizes of rectangular divisions.

By placing the celluloid over-lay on any one of the primary rectangular divisions of the quadrangle map, any point on the division can be read as a four point decimal. The fifth decimal can be estimated if desired and will locate the point to within approximately a 250 foot radius. Since each quadrangle already bears a name (printed on the map), this name precedes the decimal code in specifying locations, as, for example: "Ellicott .99887."

For field use, the author has found it convenient to cut each topographical map into its nine primary divisions and paste these into a loose-leaf notebook of appropriate size where each is labeled with the name of the quadrangle from which it was cut and the proper primary division number, as, for example: "Ellicott .9." Through the use of these maps in the field, specific locations are determined and recorded at the time of collecting each specimen.

Fortunately, the over-lay described above can be used on the soil maps which are published by the Bureau of Chemistry and Soils, United States Department of Agriculture, and which are scaled one inch to the mile. For field use, as well as for other kinds of uses, it is convenient to mount the soil maps in the same loose-leaf form referred to above, and with each map opposing the page on which the corresponding topographic map is mounted. The simultaneous use of both maps often brings to light very interesting ecological features.

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[5] J. Z. Young and P. B. Medawar, *Lancet*, 1940: 126.

[6] These experiments essentially reproduce conditions first established in tissue culture by the author (P. Weiss, *Jour. Exp. Zool.*, 68: 393, 1934) and confirm the guiding effect of an oriented fibrin matrix on nerve fiber growth.

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